Remarks

Claims 44-135 and 139-230 have been canceled without prejudice or disclaimer, and claims 41 and 136 have been amended to recite only SEQ ID NO:48. Further, claims 231 to 250 have been added. Claims 231-250 correspond to claims 71-72, 74, 115, 117-118, 120, 166-167, 169, 210, 212-213, and 215, and in part to dependent claims 42-43 and 137-138. These amendments are fully supported by the specification as filed as detailed below, and thus no new matter has been added.

Claims 41-43, 136-138, and 231-250 are pending. The Examiner has indicated that claim 69 would be allowable if rewritten in independent form. Applicants note that independent claim 41, from which claim 69 depended, has been amended to refer only to the subject matter of claim 69. Further, the Examiner made no specific rejection to dependent claims 42-43. Accordingly, Applicants respectfully submit that claims 41-43 are in condition for allowance.

Applicants thank the Examiner for the reconsideration and withdrawal of the previous restriction requirement.

I. Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

The Examiner has rejected claims 136-230 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *See* Paper No. 10, page 3. In particular, the Examiner contends that "[t]he specification as originally filed does not disclose the concept of inhibiting the activation or mobilization of basophils using the peptides recited in the claims. The concept is not specifically disclosed, and does not flow naturally from the specification." *Id.*

In response, Applicants respectfully disagree and traverse. Preliminarily, Applicants apologize for the failure to more clearly identify the support for claims 136-230 in the preliminary amendment; such support is identified below. Applicants also note that claims 139-230 have been canceled without prejudice or disclaimer, thereby mooting any rejection of such claims. However, Applicants respond to the instant rejection as it may be applied to pending claims 136-138 and 241-250.

Original claim 18 specifically recites a method "wherein said polypeptide inhibits activation or moblization [sic] of basophils." The antecedent polypeptide for claim 18 includes the polypeptides recited in the claims, such as Pro (4) to Arg (73) of SEQ ID NO:2, *i.e.*, SEQ ID NO:48. *See* original claims 1 and 6. Thus, the specification specifically claims the concept of inhibiting the activation or mobilization of basophils using the peptides recited in the present claims.

Moreover, the specification teaches that CkB-6 acts as a chemoattractant for both eosinophils and basophils. *See* pages 11-12 (description of Figures 10-12), and 106-107 (Examples 10-11). The specification also teaches that negative dominant mutants of Ckβ-6, such as the polypeptide antagonists recited in the claims, bind to the Ckβ-6 receptor (CCR3), but fail to activate the cells to which they bind. *See* page 41, lines 5-29, and page 65, line 24 to page 66, line 6. The specification further teaches that basophils express CCR3. *See, e.g.*, page 107 (Example 11). Based on the above, the specification discloses methods for using such antagonists inhibit the activation or mobilization of basophils, including:

> The antagonists may be employed to treat inflammation by preventing the attraction of eosinophils or basophiles [sic] to a wound or a site of trauma, and to regulate normal pulmonary macrophage populations, since acute and chronic inflammatory pulmonary diseases are associated with sequestration of mononuclear phagocytes in the lung. They may also be employed to treat rheumatoid arthritis, since MCP levels were found to be significantly elevated in synovial fluid from rheumatoid arthritis patients which suggests that synovial production of Ckβ-6 attracts eosinophils or basophils whose influx and activation are important in the pathogenesis of both degenerative and inflammatory arthropathies.
>
> The antagonists may also be employed to prevent allergies, since it has been shown that MCPs directly induce histamine release by basophils. Related immunological disorders including late phase allergic reactions, chronic urticaria, and atopic dermatitis can be treated by antagonists which are effective to inhibit chemokine-induced mast cell and basophil degranulation and release of histamine. ...
>
> Antagonists may also be employed to treat rheumatoid arthritis by preventing the attraction of eosinophils and basophils into synovial fluid in the joints of patients.
>
> Page 67, line 13 to page 68, line 9.

Thus, the specification specifically discloses and claims the concept of inhibiting the activation or mobilization of basophils using the peptides recited in the present claims. Applicants respectfully assert that one skilled in the art would reasonably conclude that the inventors had possession of the claimed methods of inhibiting both eosinophils and basophils upon reading the specification as filed. Therefore, the instant rejection under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description should be reconsidered and withdrawn.

II. Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

The Examiner has rejected claims 41-68 and 70-135 under 35 U.S.C. § 112, first paragraph, as allegedly not enabling a person skilled in the art to make and use the invention commensurate in scope with the claims. *See* Paper No. 10, pages 3-5. In particular, the Examiner accepts that the specification is enabling for the claimed invention wherein a polypeptide consisting of SEQ ID NO:48 is administered, but contends that it "does not reasonably provide enablement for administration of any other polypeptides to inhibit the activation or mobilization of eosinophils." Applicants presume that the Examiner also intended the assertion to apply to the activation or mobilization of basophils. Specifically, the Examiner notes that the specification teaches that SEQ ID NO:48 (residues 4-73 of SEQ ID NO:2) inhibited chemotaxis of eosinophils *in vitro*, but contends that the specification provides "no guidance regarding what sequences other than those three amino acid residues can be deleted without loss or change of activity."

In response, Applicants respectfully disagree, and assert that the previously pending claims are fully enabled by the specification in accordance with 35 U.S.C. § 112, first paragraph. However, Applicants note that claims 44-135 and 139-230 have been canceled without prejudice or disclaimer, rendering any rejection of those claims moot. Further, claims 41 and 136 have been amended to recite only SEQ ID NO:48 (which the Examiner has agreed is enabled), thus obviating the rejection as to claims 41-43 and 136-138. Applicants respond to the instant rejection as it may be applied to new claims 231-250, which recite SEQ ID NOS:50, 51, 53, 94, 96, 97, and 99.

The test for enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information

known in the art without undue experimentation. *See, e.g.*, M.P.E.P. § 2164.01(a). In the instant case, Applicants note that the Examiner has not addressed page 41, lines 5-15 of the specification, which teaches that:

> The present invention further relates to Ckβ-6 antagonists. In particular, a deletion of the first three N-terminal amino acid residues of the mature Ckβ-6 protein (i.e., a deletion of Val(1) to Ile(3) in SEQ ID NO:2) results in a polypeptide having antagonistic activity. Thus, according to the present invention, Ckβ-6 antagonists are provided wherein the amino terminus is residue 4 of SEQ ID NO:2 and the carboxyl terminus is residue m, wherein m is any residue of SEQ ID NO:2 from residue 48 to residue 93. Specific Ckβ-6 antagonists according to the present invention include, but are not limited to: Pro(4) to Arg(73); Pro(4) to Arg(75); Pro(4) to Ala(76); Pro(4) to Ala(78). Optionally, the Ckβ-6 antagonists of the present invention can include a Met residue at the N-terminus.

Thus, Applicants respectfully disagree with the Examiner, and note that specific guidance is given as to which polypeptides sequences act as antagonists capable of inhibiting eosinophil or basophil activation or mobilization. Moreover, the specification teaches several assays for verifying that a particular Ckβ-6 antagonist as described above inhibits eosinophil or basophil activation or mobilization, including an *in vitro* chemotaxis assay as described in Example 10, an *in vitro* calcium (Ca^{2+}) release assay as described in Example 9, and an *in vivo* assay as described in Example 12. *See* pages 105-108. The use of such assays would be routine by one skilled in the art. While the Examiner has specifically noted the results of these assays as regarding SEQ ID NO:48, only a cursory assertion has been made as to why it would constitute undue experimentation for one skilled in the art to verify the remaining antagonists using the disclosed assays.

Applicants also point out that 35 U.S.C. § 112, first paragraph, only requires that Applicants enable what is claimed. As noted above, the scope of the pending claims is not identical to the previously pending claims. In particular, Applicants point out that claims 231-250 are directed to SEQ ID NOS: 50, 51, and 53, corresponding to the specific Ckβ-6 antagonists described above other than SEQ ID NO:48, and to SEQ ID NOS:94, 96, 97, and 99, which correspond to SEQ ID NOS:48, 50, 51, and 53 with the addition of a Met residue at the N-terminus. In light of the guidance given in the specification that "a deletion of Val(1) to Ile(3) in SEQ ID NO:2 results in a polypeptide having antagonistic

activity," and the specific description of SEQ ID NOS: 48, 50, 51, 53, 94, 96, 97, and 99 as antagonists at page 41, lines 5-15, the pending claims are fully enabled.

Accordingly, Applicants assert that the pending claims are in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

Conclusion

Entry of the above remarks is respectfully solicited. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

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